

Ultrasound-Guided Atelocollagen Injection for Chronic Pain After Spinal Surgery: A Retrospective Cohort Study

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Background: Chronic pain after spinal surgery (CPSS), formerly known as failed back surgery syndrome (FBSS), is a persistent and complex condition that often resists conventional treatments. Recent attention has turned toward paraspinal muscle degeneration as a contributing factor. Injectable type I porcine atelocollagen, known for its anti-adhesive and regenerative properties, has been proposed as a potential intervention, but clinical evidence remains scarce. This study aimed to evaluate the effect of ultrasound-guided atelocollagen injection into paraspinal muscles for patients with CPSS and to identify potential predictors of treatment response.

Methods: This single-center retrospective cohort study was conducted at a tertiary academic institution. 34 adult patients (≥ 20 years) with a diagnosis of lumbosacral CPSS who received ultrasound-guided purified porcine atelocollagen injections between October 2020 and December 2023 and completed 3-month follow-up without concurrent interventional procedures or medication escalation were included in the analysis. The injection was performed into the paraspinal muscles at the surgical level. The primary outcome was change in pain intensity on the 11-point numeric rating scale (NRS) at 3 months post-treatment. A composite outcome was defined as a ≥ 1 -point reduction in NRS or a Patient Global Impression of Change (PGIC) score of 4 or 5. Exploratory analyses were conducted to identify potential predictive factors.

Results: The mean NRS score significantly decreased by 1.62 points (95% CI 0.91–2.33, $p < 0.001$) at 3 months after atelocollagen injection compared to baseline. Neither univariable nor multivariable logistic regression analysis revealed any significant predictive factors for a positive composite outcome. When comparing the responder and non-responder groups based on the composite outcome, the proportion of patients taking anticonvulsants or antidepressants was significantly higher in the non-responder group (54.2% vs 100%, $p = 0.028$).

Conclusion: Ultrasound-guided atelocollagen injection into the paraspinal muscles was associated with pain reduction in patients with CPSS. Although the absence of a control group limits causal interpretation, this suggests that atelocollagen injection may have potential as an adjunctive or investigational treatment option for this patient population.

Keywords: atelocollagen, ultrasonography, interventional, persistent spinal pain syndrome, paraspinal muscles, chronic pain

Introduction

Chronic pain after spinal surgery (CPSS) is the term now used to describe a clinical condition previously labeled as “failed back surgery syndrome” (FBSS). In 2019, the International Association for the Study of Pain (IASP) formally defined FBSS as “lumbar spinal pain of unknown origin either persisting despite surgical intervention or appearing after surgical intervention for spinal pain originally in the same topographical location”. Accordingly, the term CPSS has been adopted and is now included in the ICD-11 classification.¹ CPSS affects approximately 10% to 20% of patients who undergo spinal surgery and represents a growing contributor to long-term disability and healthcare utilization.^{2,3}

Current management strategies for CPSS involve pharmacological treatments, epidural steroid injections, neuromodulation, and revision surgeries. However, according to the literature, the causes of CPSS are diverse, and in approximately 10% of cases, the cause cannot be identified.^{4–8} In some patients, paraspinal muscle degeneration and fibrosis—often resulting from surgical trauma or suboptimal healing—may contribute to ongoing pain. Although such structural changes are frequently observed on imaging studies, they are not commonly emphasized in conventional CPSS treatment strategies.^{9–12}

Type I porcine atelocollagen, a purified collagen biomaterial with reduced immunogenicity achieved by enzymatic removal of telopeptides, has been investigated for its potential regenerative effects. Both experimental and clinical research suggest that atelocollagen may inhibit fibro-adhesive scar tissue formation, promote organized tissue repair, and reduce soft tissue adhesions.^{13–17} Mechanistically, atelocollagen is thought to function as a biocompatible scaffold that supports fibroblast proliferation and collagen remodeling, while modulating local inflammatory and cytokine responses.^{18,19} In the paraspinal region, these effects could potentially attenuate postoperative fibrosis and muscle degeneration by restoring extracellular matrix integrity and improving microcirculatory exchange. In orthopedic applications, ultrasound-guided injections of atelocollagen have shown improvements in pain and joint function in conditions such as rotator cuff injuries and knee osteoarthritis, with a favorable safety profile.^{20–24} In addition, a pilot study showed that this approach may have the potential to prevent paraspinal muscle atrophy during the early postoperative period.²⁵ Although these initial findings are encouraging, the application of ultrasound-guided paraspinal atelocollagen injection (PAI) in patients with CPSS has yet to be investigated in the published literature.

In this retrospective cohort study, we evaluated changes in pain over a 3-month period following ultrasound-guided PAI in patients with CPSS who had demonstrated an inadequate response to conventional therapies. We also examined baseline clinical characteristics associated with achieving a composite clinical response, which we defined as a combination of measurable pain reduction and patient-reported improvement, to identify potential predictive factors.

Materials and Methods

Study Design and Ethical Approval

We conducted a single-center, retrospective cohort study at Seoul National University Hospital, a tertiary academic institution in Seoul, Korea. The study protocol complied with the Declaration of Helsinki and was approved by the hospital's Institutional Review Board (IRB No. 2401–133–1505). Because the analysis relied exclusively on de-identified chart data, the requirement for individual informed consent was waived.

Patient Selection

Electronic medical records were reviewed to identify adults (≥ 18 years) with a diagnosis of chronic pain after spinal surgery (CPSS) who received ultrasound-guided injections of 3% purified porcine type I atelocollagen into the lumbar paraspinal muscles between October 2020 and December 2023, and who completed at least 3 months of follow-up after the final injection. Since CPSS was not yet registered as a diagnostic code in the hospital system at the time, patients whose diagnoses were recorded as either FBSS or Post Spinal Surgery Syndrome (PSSS) and who reported pain persisting for more than 3 months were included. Patients were excluded when any of the following applied: hypersensitivity to atelocollagen, active infection at the intended injection site, receipt of another lumbosacral interventional procedure within 3 months before or after the atelocollagen injection, documented escalation of adjuvant pain medications during the same interval, loss to follow-up, or incomplete baseline or outcome data.

Ultrasound-Guided Paraspinal Atelocollagen Injection Technique

All procedures were performed in a dedicated ultrasound room equipped with point-of-care ultrasound by pain physicians who had completed a fellowship. The patient was placed in the prone position with a pillow positioned under the abdomen to increase the distance between the lower ribs and the iliac crest. Following sterile preparation of the procedural site, a sterile drape was applied. Two ultrasound systems were utilized: the V6 (Samsung Healthcare, Seoul, Republic of Korea) or the Epiq Evolution 3.0 (Royal Philips N.V., Amsterdam, Netherlands). A 1–7 MHz curved ultrasound probe was enclosed in a sterile cover.

Prior to the procedure, the patient's medical records and imaging studies were reviewed to confirm the level and type of prior spinal surgery. The skin was also inspected for the presence of surgical scars. All atelocollagen injections were performed under ultrasound guidance. To minimize post-injection discomfort, 1 mL of 3% purified porcine type I atelocollagen was mixed with 5 mL of 1% lidocaine, resulting in a total volume of 6 mL. The surgical region was divided into three segments, resulting in six injection sites, with three on each side of the lumbar spine. At each site, a 23-gauge needle was inserted from the lateral skin surface and advanced medially to the depth of the paraspinal muscles (Figure 1). Figure 1 illustrates both the ultrasound-guided needle trajectory used for the atelocollagen injection and the comparative paraspinal muscle morphology between healthy individuals and patients with chronic persistent spinal pain syndrome, providing anatomical context for the procedure. The injectate was delivered at the point where tissue resistance decreased during slow needle withdrawal. A volume of 1 mL was injected at each of the six designated sites. Atelocollagen injections were administered up to three times per patient, depending on clinical response.

Data Collection

Demographic variables (age, sex, body mass index), comorbidities, details of the index spinal surgery, pain duration and time since surgery, baseline analgesic regimen, and the number of atelocollagen sessions were extracted from the electronic medical records. 11-point Numeric rating scale (NRS; 0 = no pain, 10 = worst pain imaginable) and 5-point Patient Global Impression of Change (PGIC) scores, recorded at baseline and at routine outpatient follow-ups (approximately every 2 to 4 weeks), were retrospectively collected for analysis. PGIC is a patient-reported outcome measure that assesses the patient's overall perception of improvement after treatment. It consists of a 5-point scale: (1) worsened, (2) no change, (3) minimally improved, (4) much improved, (5) very much improved. Patients select the category that best describes their impression of change since the procedure.

Outcomes

The primary outcome was the change in lumbar pain intensity, assessed with an NRS score at 3 months after the last injection compared with baseline. Secondary outcomes included the proportion of composite responders, defined as patients who achieved a ≥ 1 -point reduction in NRS score or reported being "very much improved" or "much improved" on the 5-point PGIC. Because patients with CPSS who do not respond to conventional treatments often experience persistent and long-lasting pain, patient satisfaction with treatment cannot be fully explained by a reduction in NRS scores alone. Therefore, a composite outcome measure was established to better capture the overall clinical improvement. Procedure-related adverse events were also recorded up to the final follow-up visit.

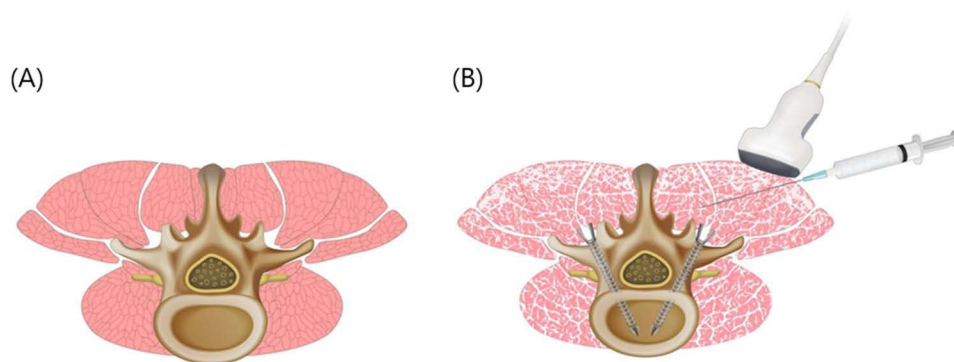


Figure 1 Schematic illustration depicting both the ultrasound-guided injection trajectory and the paraspinal muscle morphology. (A) shows a healthy control with normal paraspinal muscle bulk and minimal fatty infiltration. (B) shows a patient with chronic persistent spinal pain syndrome (CPSS), demonstrating characteristic degeneration including atrophy, fatty infiltration, and fibrosis, along with the illustrated needle trajectory used for atelocollagen injection.

Statistical Analysis

All statistical analyses were performed using R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). The Shapiro–Wilk test was used to assess the normality of continuous variables. Normally distributed data are presented as mean $\pm$ standard deviation and were compared using paired or unpaired *t*-tests, as appropriate. Non-normally distributed data are presented as median (interquartile range) and were analyzed using the Wilcoxon signed-rank test or the Mann–Whitney *U*-test. Categorical variables are summarized as frequencies and percentages and were compared using Fisher’s exact test or the chi-square (χ^2) test.

Exploratory univariable logistic regression was conducted to identify candidate predictors of composite response using a threshold of $P < 0.20$. Variables meeting this criterion and deemed clinically relevant were included in a stepwise multivariable logistic regression model. A two-tailed $P < 0.05$ was considered statistically significant. Given the retrospective design and exploratory nature of the study, a formal a priori sample size calculation was not performed. However, a post hoc power analysis and sample size estimation were conducted based on the observed effect size. The mean NRS pain score decreased from 7.3 ± 1.8 at baseline to 5.7 ± 2.2 at 3 months, yielding an effect size of Cohen’s $d = 0.81$, which corresponds to a post hoc power of 0.996 (99.6%) for a two-tailed paired *t*-test at an α level of 0.05. The post hoc sample size calculation indicated that 13, 17, and 21 participants would have been sufficient to achieve 80%, 90%, and 95% power, respectively, assuming the same effect size.

Given the small sample size ($n = 34$) and the exploratory nature of this study, subgroup analyses and inferential statistical comparisons were excluded from the main text and are presented in [Supplementary Table 1](#) and [Supplementary Figure 1](#).

Results

Study Cohort

Of the 165 records screened, 109 were excluded based on the inclusion and exclusion criteria, and 22 were found to be ineligible for the study, leaving 34 patients for analysis ([Figure 2](#)). Baseline demographic and surgical details

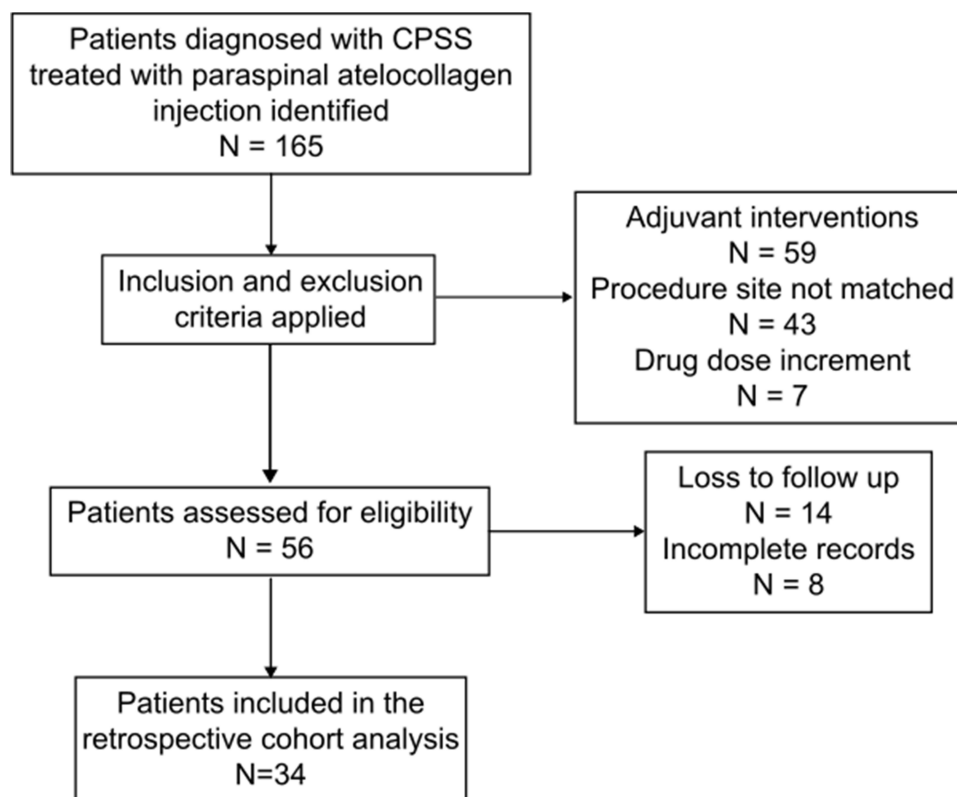


Figure 2 Diagrammatic overview of the patient inclusion process.

are presented in Table 1. The cohort was predominantly female (73.5%) with a mean age of 72.1 ± 12.1 years and body-mass index (BMI) $25.7 \pm 3.6 \text{ kg m}^{-2}$. Most operations were open procedures (79.4%) including open interbody fusion, laminectomy, discectomy. The remaining 20.6% underwent minimally invasive surgery such as endoscopic decompression, endoscopic discectomy, or vertebroplasty. Mean pain duration was 46.5 ± 53.5 months. The interval from surgery to first injection averaged 102.6 ± 88.0 months, and baseline NRS score was 7.3 ± 1.8 .

Primary Outcome

The mean NRS pain score was 7.3 ± 1.8 at baseline. At the 3-month follow-up, the average score had declined to 5.7 ± 2.2 , indicating a significant reduction in pain intensity (Table 2 and Figure 3). This change was statistically significant (95% CI, 0.91–2.33; $p < 0.001$). The calculated effect size (Cohen's $d = 0.81$) also indicated a statistically significant improvement.

Secondary Outcomes

Using the composite responder definition (≥ 1 -point NRS score reduction and Patient Global Impression of Change, PGIC ≥ 4), 24 patients (70.6%) met the composite response criteria (Table 2). The mean PGIC score at 3 months was 3.1 ± 1.1 . Additionally, 17 patients (50%) achieved either a ≥ 2 -point reduction in NRS score or a reduction in adjuvant analgesic use. Among this responders, 2 patients (5.9%) were able to reduce their use of adjuvant medications.

Safety

Five patients (14.7%) experienced mild, self-limited soreness at the injection site. There were no reports of other adverse events during the 3-month follow-up.

Table 1 Demographics and Baseline Characteristics

	Patients (n = 34)
Age (years)	72.1 ± 12.1
Sex, male/female (%)	9 (26.5) / 25 (73.5)
BMI (kg/m^2)	25.7 ± 3.6
Comorbidity (%)	
Hypertension	14 (41.2)
Diabetes Mellitus	7 (20.6)
Smoking (%)	1 (2.9)
Type of spine surgery (%)	
Open Surgery [†]	27 (79.4)
Minimally Invasive Surgery [†]	7 (20.6)
Pain duration (months)	46.5 ± 53.5
Duration between surgery and injection (months)	102.6 ± 88.0
Analgesics (%)	
Anticonvulsants or Antidepressants	23 (67.6)
Weak opioid	10 (29.4)
Strong opioid	8 (23.5)
Non-opioid analgesics	19 (55.9)
Morphine milligram equivalent / day	18.9 ± 29.9
11-point NRS pain score (0–10)	7.3 ± 1.8
Number of injections	2.56 ± 0.7

Notes: Data are presented as a number and proportion (%) for categorical variables or categorical variables or mean $\pm$ SD.[†] Open surgery includes Open Interbody Fusion (23, 67.6%), Open Laminectomy (2, 5.9%), and Open Discectomy (2, 5.9%) while Minimally Invasive Surgery includes Endoscopic Decompression (4, 11.8%), Endoscopic Discectomy (1, 2.9%), and Vertebroplasty (2, 5.9%). The percentage represents the proportion relative to the total study population.

Abbreviations: BMI, body mass index; NRS, numerical rating scale.

Table 2 Clinical Variables at 3 months After the Paraspinal Atelocollagen Injection

	Patients Who Underwent the PAI (n = 34)
11-point NRS pain score (0–10)	5.7 ± 2.2*
Positive Response (%) ¹	24 (70.6)
Open Surgery	18 (75.0)**
Minimally Invasive Surgery	6 (25.0)**
Morphine milligram equivalent / day	18.9 ± 29.9
PGIC (0–5)	3.1 ± 1.1
Dose Reduction of Adjuvant Analgesics ²	2 (5.9)

Notes: Data are presented as a number and proportion (%) for categorical variables or mean ± SD.

*Significant differences were observed through a paired t-test ($P < 0.05$). **Percentage within the positive response group. ¹Positive Response were defined as participants whose 11-point NRS pain score decreased by at least 1 point from baseline and who indicated much improved or somewhat improved on the 5-point Likert scale PGIC (scores 5 and 4, respectively). ²Discontinuation of adjuvant analgesics was observed in two patients—pregabalin in one case and amitriptyline in another.

Abbreviations: PAI, paraspinal atelocollagen injection; PGIC, patient global impression change.

Discussion

In this retrospective cohort study of 34 patients with CPSS, over a 3-month period, the mean NRS score decreased by 1.62 points, and 70.6% of patients met the composite responder definition, which combined at least a 1-point NRS score reduction with a PGIC rating of “much improved” or “very much improved”. Additionally, 50% of the cohort experienced either a ≥ 2 -point reduction in NRS score or a decrease in the dose of adjuvant analgesics. The absence of serious adverse events in this cohort suggests that the procedure may carry a relatively low risk profile. These findings suggest that ultrasound-guided paraspinal delivery of atelocollagen may provide clinical benefit for a subset of CPSS patients who are refractory to conventional conservative treatments. However, further well-designed studies are warranted to confirm these results.

Comparison with Existing Evidence

While atelocollagen has been widely explored in preclinical and clinical contexts for its regenerative potential, its role in spine-related chronic pain remains relatively underexplored.^{14,15,20,21,24–32} Although atelocollagen has been utilized in orthopedic and soft tissue repair, its application to spinal disorders has been limited and remains an area of ongoing investigation.^{33–38} Preclinical studies have demonstrated its utility as a biological scaffold promoting cell differentiation and tissue regeneration across various tissues including tendons, muscles, and cartilage. In human studies, randomized

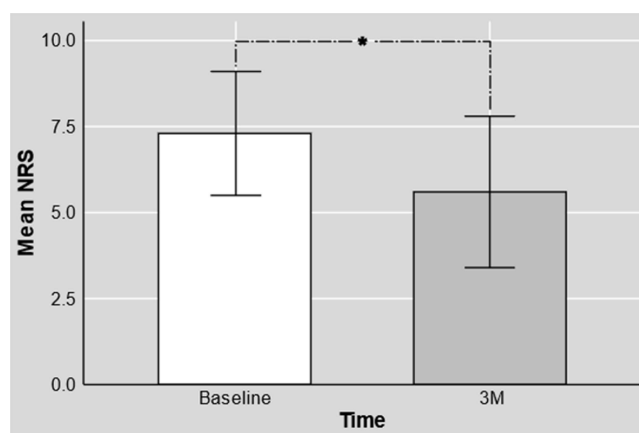


Figure 3 Bar plot comparing the baseline mean 11-point numeric rating scale (NRS) and the NRS at 3 months (3M). The asterisk (*) indicates that the mean NRS showed a statistically significant difference when a paired t-test was performed (95% CI: 0.91–2.33, $p < 0.001$).

controlled trials have shown mixed results: intra-articular atelocollagen led to functional and symptomatic improvements in knee osteoarthritis, while surgical application in rotator cuff and ankle cartilage repair improved structural healing but did not consistently enhance pain or functional scores.^{27,32,38} Although a previous study applied atelocollagen to the paraspinal muscles of patients with low back pain, it evaluated its use as an adjuvant to lumbar interlaminar epidural steroid injection (LESI).³⁹ In that study, the group receiving atelocollagen demonstrated an additional reduction in NRS pain score of 0.66 points compared with the LESI-only group ($p < 0.001$; Cohen's $d = 0.40$). Also, the study involved a heterogeneous patient population and used fluoroscopic guidance, limiting direct comparison to our ultrasound-guided approach in a CPSS cohort. Our study has several strengths. First, we restricted enrollment to patients with CPSS, a population often considered challenging to treat with standard interventions. Second, we excluded individuals who had received other interventional pain procedures within three months before or after the injection, and those who had escalation of their medication regimen within three months after the injection, minimizing confounding effects. Third, the use of ultrasound guidance enabled direct visualization of the paraspinal muscles, allowing relatively precise delivery of atelocollagen into the intended anatomical targets adjacent to the surgical site.

Potential Mechanisms

The mechanisms by which atelocollagen exerts therapeutic effects in chronic post-surgical tissue remain speculative. Telo peptide-cleaved collagen matrices have been shown to reduce fibroblast proliferation, modulate macrophage activity, and support organized muscle regeneration.^{13,16,17,40,41} In the context of CPSS, these properties may counteract fibrosis and architectural disruption of the paraspinal musculature, restoring functional tissue integrity and reducing nociceptive drive. Many previous studies evaluating the effects of atelocollagen in both animal and human models applied it during the early phase of tissue injury.^{13,25,42} The reported effects, including reduced fibroblast proliferation and enhanced tissue regeneration, appear to have been most consistently demonstrated under acute injury conditions. In contrast, patients with CPSS are unlikely to be in the acute phase of paraspinal muscle injury, which may partially account for the variability in therapeutic response observed among individuals in this population.^{43,44} It is also possible that, beyond the mechanisms previously described, atelocollagen exerts its effects through additional, as yet unidentified, pathways. Seong et al suggested that atelocollagen, due to its resistance to degradation, may persist at the injection site and occupy space in a way that attenuates inflammatory responses and mitigates mechanical stress associated with repetitive movement.²² While this is theoretically plausible, objective evidence remains limited. In our experience, follow-up imaging at 1 month post-injection revealed that in some cases, the muscle defect was replaced by another material, suggesting that the injected collagen may act as a scaffold and interact with surrounding tissues. However, the exact nature of these sonographically observed changes remains unclear and would require biopsy confirmation through animal studies.

Limitations

This study has several limitations. Its retrospective and single-arm nature may have led to selection bias and limits the ability to draw firm conclusions about causality.^{45,46} The relatively small sample size reduced statistical power for multivariable analyses. Although strict exclusion criteria were applied to minimize confounding, a considerable number of patients were excluded from the initial cohort of 165, leaving only 34 in the final analysis. Because the number of atelocollagen applications differed according to each patient's clinical response, establishing a consistent dose-response relationship was not feasible. These factors should be considered when interpreting the results. Also, the mean reduction in NRS observed in this study may not exceed the commonly accepted threshold for the minimal clinically important difference (MCID), and the within-group design of this study should be taken into consideration. Nevertheless, this degree of improvement could still be meaningful for patients with chronic, treatment-refractory pain who have not responded to conventional therapies. Functional outcomes, such as quality of life or disability indices (eg, Oswestry Disability Index), were not uniformly captured. Additionally, the lidocaine admixture, while intended to reduce post-injection discomfort, confounds attribution of efficacy solely to the atelocollagen scaffold. Finally, potential mechanical or trigger-point effects from needling could not be excluded.^{47–50}

Future Directions

Prospective randomized controlled trials (RCTs) and long-term follow-up data along with careful patient selection are necessary to establish treatment safety, efficacy, define optimal injection parameters, and clarify which subgroups of patients are more likely to benefit. Imaging tools such as ultrasound elastography or MRI-based assessments of paraspinal muscle condition may help link anatomical characteristics with clinical outcomes.^{50–53}

Conclusions

Ultrasound-guided paraspinal atelocollagen injection was associated with a measurable reduction in pain and a favorable safety profile in patients with CPSS. While preliminary in nature, these findings indicate that atelocollagen may represent a promising area for further investigation in the management of CPSS. Well-designed prospective studies are warranted to validate these preliminary results and clarify their clinical implications.

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Disclosure

The authors declare no conflicts of interest in this work.

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